

REMARKS

The present response is submitted in reply to the Final Office action issued on October 19, 2005. Claims 33-43 are pending in this application. By the present response, no claims have been amended. No new matter has been added. Reconsideration is respectfully requested in light of the following remarks.

Rejection of claims 33-43 under 35 U.S.C. 112, first paragraph

Claims 33-43 have been rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement. The Examiner states that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner acknowledges that the specification has support for three polymer layers (Fig. 1 of the specification) but that the specification only provides support for a system that has two layers with different glass transition temperatures and not three. The Examiner states that the recitation “the glass transition temperature Tg1 ...are identical *or different*...” does not have support since there is only support for the first layer and third layer having identical glass transition temperatures. Therefore, the Examiner considers the term “different” to be new matter.

The applicant respectfully disagrees and submits that the original disclose clearly provides support for both instances, namely: (1) where the system has three layers and the polymer of the first and third layers have the same Tg while the polymer of the second layer has a second Tg; and (2) where the system has three layers and all three layers have

a polymer having a different Tg. The applicant agrees with the Examiner that the specification and Fig. 1 support the former Tg configuration. However, the applicant again respectfully submits that the specification quite clearly supports the latter Tg configuration as well. As noted in the previous response, page 9, lines 1-2 of the specification recite “The various layers **differ** (emphasis added) in their glass transition temperature (Tg).” On page 10, lines 1-5, the specification clearly recites “... at least two polymer-containing layers upon one another, with the layers containing polymers which **differ** (emphasis added) in their glass transition temperature.” Moreover, original claims 1 and 5 recite in part “...the polymers used for the different layers **differ** (emphasis added) in their glass transition temperature” and “...layers containing polymers that **differ** (emphasis added) in their glass transition temperature.” Still further, the Abstract as filed recites in part “...at least two polymer-containing layers, characterized in that the polymer used for the different layers **differ** (emphasis added) in their glass transition temperature.” In light of the aforementioned passages of the present specification, the applicant respectfully submits that the specification provides sufficient support for a system having three layers, where the first layer has a polymer with Tg1, the second layer has a polymer with Tg2 and the third layer has a polymer with Tg3 and where Tg1 and Tg3 may be different.

The applicant also wishes to note that nowhere in the specification it is recited that it is critical for Tg1 and Tg3 to be identical. The applicant submits that the main reason why this particular embodiment (where Tg1 and Tg3 are identical) was selected in the Example was because it can be produced most easily and inexpensively. Withdrawal

of this rejection is respectfully requested.

Rejection of claims 33-43 under 35 U.S.C. 103(a)

Claims 33-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,151,271 (Otsuka et al.) by itself or in view of U.S. Patent No. 6,063,838 (Patnode, et al.). According to the Examiner, Otsuka teaches a pressure sensitive adhering composite medicinal preparation to provide drug supply to the skin comprising every limitation set forth in the present claims, except for the third layer. The Examiner states that Otsuka, et al. does teach at least (emphasis provided) two layers, namely at least one pressure-adhering macromolecular layer substance layer and polymer layer adjacent to the macromolecular substance layer. However, the Examiner notes that although Otsuka, et al. suggest more than two polymer layers, the reference does not exemplify the third layer. It is the Examiner's position that it would have been obvious to one skilled in the art to refer to Otsuka, et al. and incorporate a third polymer-containing layer with the motivation being that Otsuka, et al. teaches that the composite should contain at least two layers.

The Examiner refers to Patnode, et al. for the teaching of a blended pressure-sensitive adhesive which is formed from at least two polymeric materials wherein at least one is a pressure sensitive adhesive. The Examiner further states that the reference teaches an embodiment wherein a multilaminate device contains a backing, an adhesive layer which contains the drug and excipients, a membrane that controls the rate at which the drug is diffused to the skin, a second adhesive layer and a release layer. The Examiner concludes that it would have been obvious to one skilled in the art to combine

the teachings of Otsuka, et al. and Patnode, et al. to utilize a third layer and to arrive at the present invention as set forth in present claims 33-43.

Claims 33-43 are also rejected as being unpatentable over Otsuka, et al. by itself or in view of U.S. Patent No. 5,023,084 (Chien, et al.). As mentioned above, the Examiner states that Otsuka, et al. teaches every limitation of claims 33-43 but does not exemplify the third layer. It is the Examiner's position that it would have been obvious to one skilled in the art to refer to Otsuka, et al. and incorporate a third polymer-containing layer with the motivation being that Otsuka, et al. teaches that the composite should contain at least two layers.

The Examiner further refers to Chien, et al. for the teaching of a transdermal system that provides a combination of drugs (estrogen and progestin) in a unit dosage. According to the Examiner, Example 8 of Chien, et al. teaches that the transdermal contains a first adhesive layer that contains the estrogen and a pressure sensitive adhesive, a separating layer containing polyisobutylene polymer and a third adhesive layer that contains the progestin and a pressure sensitive adhesive. The Examiner concludes that it would have been obvious to one skilled in the art to combine the teachings of Otsuka, et al. and Chien, et al. to utilize another macromolecular layer which has a lower glass transition temperature than the polymer layer, thereby arriving at the present invention as set forth in present claims 33-43.

The applicant respectfully submits that to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation to modify the reference or to combine the reference teachings. Second, there

must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all of the claim limitation. Applicant respectfully submits that one skilled in the art would have no suggestion or motivation to combine the aforementioned references in order to arrive at the present invention. Additionally, even if one skilled in the art were to consider Otsuka et al. alone, or in combination with either of Patnode, et al. or Chien, et al., each and every limitation of the present invention would not be disclosed, nor would there be a reasonable expectation of success if the aforementioned references were to be considered alone, or in combination.

The applicant first submits that Otsuka, et al. does not provide a clear teaching according to which it would be essential that the polymer of the polymer layer has a Tg that is higher than the Tg of the polymer of the macromolecular layer. The Examiner refers to the glass transition temperatures taught by Otsuka, et al. in connection with the polymer layer and macromolecular layer and compares the same to the layers of the present invention. Otsuka, et al. indicates that the range for the polymer layer (which apparently corresponds to the layer Tg2 of the present invention) is somewhat higher than the range indicated by Otsuka, et al. for the macromolecular layer (i.e., “not lower than -50°C” vs. “not lower than -70°C;” col. 2, line 24; col. 3, line 15, respectively). In light of this recitation of Otsuka, et al., as noted above, Otsuka, et al. does not provide a clear teaching according to which it would be essential that the polymer of the polymer layer has a Tg that is higher than the Tg of the polymer of the macromolecular layer. For example, example 3, which is in accordance with the invention set forth by Otsuka, et al., relates to a composition in which the skin-adhesive layer, which may be compared to the

layer Tg1 of the present invention, has a Tg that is higher than the Tg of the macromolecular layer, which may be compared to the layer Tg2 of the present invention. Taking Otsuka, et al. in its entirety, the reference clearly is vague on whether or not it is essential for the Tg of the polymer layer to be higher than the Tg of the macromolecular layer.

The applicant further submits that it is simply not clear to one skilled in the art whether Otsuka, et al. suggests more than two polymer layers, as suggested by the Examiner on page 5, lines 19-20 of the Office action. Referring to column 2, lines 5-9 of Otsuka, et al., the preparation of Otsuka, et al. comprises “at least two layers, namely (emphasis added) a layer of a macromolecular substance ... and a polymer layer.” As a third or further layer, a supporting sheet may be provided (col. 2, lines 63-65; claim 11). However, Otsuka, et al. does not clearly suggest using a polymer layer (comprising a polymer with a Tg not lower than -50°C) as a third or further layer. In fact, Otsuka, et al. is clear that a third layer would be a film or sheet on one side of the polymer layer (col. 2, lines 63-64). Based on the Examples and the specification provided by Otsuka, et al., one skilled in the art would believe that the preparation of Otsuka, et al. comprises a single macromolecular layer, a single polymer layer and a supporting sheet (and possibly a release liner (col. 6, line 20)).

The Examiner further supports her position by stating that on page 6, lines 1-2 of the Office action, Otsuka, et al. teaches that the composite thereof contains “*at least* (emphasis provided) two layers and in particular *at least one* (emphasis provided) macromolecular layer.” The applicant strongly disagrees with this interpretation of

Otsuka, et al. According to the teaching of Otsuka, et al., it is essential that the drug compound and the absorption-enhancing compound are present in different layers of the composite preparation (col. 6, lines 22-26). In accordance with this requirement, claim 1 of Otsuka, et al. specifies that “one of said layers (a) and (b) contains a ... drug and [the] other of said layers contains an adjuvant...” The passage of Otsuka, et al. in column 2, lines 5-13 has the same meaning. Otsuka, et al. recites the following at column 2, lines 4-15:

“[A] composition preparation characterized in that it comprises at least two layers, namely layer of a macro-molecular substance having pressure-sensitive adhesiveness at ordinary temperatures and a polymer layer adjacent to said macromolecular substance layer, that at least one of the macro-molecular substance layer and polymer layer at least contains a percutaneously absorbable drug and the other at least contains an adjuvant capable of increasing percutaneous drug absorption, and that the drug and adjuvant respectively can migrate into the adjacent macromolecular substance layer and polymer layer.”

The applicant respectfully submits that Otsuka, et al. teaches:

1. that there are at least two layers;
2. one of these layers is a macromolecular polymer layer;
3. another of these layers is a polymer layer;
4. the macromolecular layer and the polymer layer are adjacent to each other;
5. at least one of either the macromolecular layer and the polymer layer (i.e., the macromolecular layer) contains a drug;
6. the other layer (i.e., the polymer layer) contains an adjuvant;
7. the polymer layer is supported on one side (i.e., the side not adjacent to the macromolecular layer) by a film or sheet; and

8. the macromolecular layer may preliminarily include formation on a release liner followed by transfer of the macromolecular layer onto the polymer layer for lamination.

The teaching of Otsuka, et al. clearly does not include “at least one macromolecular layer,” but rather just a single macromolecular layer. Moreover, the applicant’s position that Otsuka, et al. fails to teach “at least one” macromolecular layer is further supported by the fact that Otsuka, et al. discusses throughout the reference “a” (or “the”) macromolecular layer (emphasis added), rather than “at least one macromolecular layer” or “macromolecular layers”) (see for instance, col. 6, lines 10, 14, 17-18, 19-20; col. 7, lines 13-14; claim 1)).

The phrase “at least one of the macromolecular substance layer and polymer layer...” means that either the macromolecular substance layer or polymer layer (or both layers) at least contains a drug and the respective other layer at least contains an absorption-enhancing adjuvant. The underlying idea is that the drug and adjuvant are initially kept separately in two different layers. However, the phrase “at least one of the macromolecular substance layer and polymer layer ...” cannot and should not be interpreted as referring to more than one macromolecular substance layer. Since Otsuka, et al. does not clearly and unambiguously teach “at least one macromolecular substance layer,” this reference does not provide a clear suggestion that more than one macromolecular layer may be used, as stated by the Examiner in the Office action (page 6, line 2; page 7, lines 21-22; page 9, line 21; page 11, lines 21-22).

Moreover, the applicant submits that the wording “at least contains a drug” and

“at least contains an adjuvant” (col. 2, lines 9-13) suggest that each of the two layers (the macromolecular layer and the polymer layer) may contain more than one drug or more than one adjuvant, or even contain multiple compounds, but regardless must contain at least one drug and the other at least one adjuvant. Therefore, even if one skilled in the art would have desired to incorporate a combination of two or more drugs into Otsuka’s preparation, that person would have added these further substances to the respective layer and would not have provided a third or further drug-containing or adjuvant-containing layer.

The applicant still further respectively submits that if it is assumed that Otsuka, et al. does suggest using two macromolecular layers, the relative position of this second macromolecular layer and the Tg of the polymer contained in this layer would not be obvious to one skilled in the art. According to Otsuka, et al., the function of the macromolecular layer is to secure the adhesion of the preparation to the skin (col. 2, lines 6-7; col. 3, lines 3-6). Therefore, there would not have been any motivation for a skilled person to have provided a second skin-adhesive layer at the opposite side of the polymer layer, as it would be unnecessary and disadvantageous to have a second skin-adhesive surface.

Moreover, throughout Otsuka, et al. and as already noted above, the polymer layer is described as being covered by a support sheet on one side (i.e., on the side that is not in contact with the macromolecular layer); (col. 2, lines 63-65; Examples). Specifically, Otsuka, et al. teaches that “[t]he above polymer layer is preferably supported, on one side thereof (emphasis added), by a film or sheet substantially impermeable to the drug and

adjuvant...” This still further supports the applicant’s position that this polymer layer was clearly not intended to be covered (or “sandwiched”) by an additional adhesive macromolecular layer, as suggested by the Examiner in the Office action at page 8, lines 3-6). Clearly, Otsuka, et al. teaches that the polymer layer would be “sandwiched” on one side by a macromolecular layer and on the other side by a film or sheet. The Examiner’s conclusion that Otsuka, et al. teaches a second macromolecular layer adjacent to the polymer layer is clearly inapposite to Otsuka, et al.’s preferred teaching that a film or sheet substantially impermeable to the drug and adjuvant be placed on one side of the polymer layer.

Regarding the Tg of the macromolecular layer, the applicant submits that the limitation provided in col. 3, lines 11-26 of Otsuka, et al., is preferred to improve the shape-holding property, to prevent residue on the skin, to prevent skin irritation and to improve skin adhesiveness (col. 3, lines 14-18). However, if a second macromolecular layer would be provided on the other side of the polymer layer (in a sandwiched configuration), as noted above, then this polymer layer would be located opposite to the skin-contacting side of the composite preparation and Tg ranges indicated in column 3 would not even be applicable in this case. Clearly, one skilled in the art would have assumed that this Tg criterion must only be observed when the macromolecular layer is a skin contact layer. Therefore, even if one skilled in the art would have considered adding a second macromolecular substance layer in a sandwich-type configuration as suggested by the Examiner, it would not have been obvious to use a layer comprising a polymer whose Tg is lower than the Tg of the center layer (i.e., Tg2 in the present invention). In

light of the numerous deficiencies of Otsuka, et al., withdrawal of this rejection is respectfully requested.

As explained above, the Examiner cites Patnode, et al. for combining with Otsuka, et al. to teach a third layer and to utilize an additional pressure sensitive layer (layer 57 of Fig. 15 of Patnode, et al.). The applicant respectfully disagrees for at least the aforementioned deficiencies of Otsuka, et al. However, the additional pressure sensitive layer 57 is functionally linked to the rate-controlling membrane 55 (Fig. 15). The multilaminate device is adhered to the skin by the adhesive surface of the pressure sensitive layer 56 that is covered by the release liner 58. The active substance present in pressure sensitive layer 57 migrates through membrane 55 and pressure sensitive layer 57 to produce a controlled migration of active substance towards the skin surface (col. 13, lines 1-28). Therefore, in the absence of a rate-controlling membrane, there would be no need or motivation for adding a second, active substance-containing adhesive layer 57.

Otsuka, et al. does not suggest that the preparations may contain a rate-controlling membrane. The function of the polymer layer is to allow diffusion and migration of a drug and adjuvant, not to restrict diffusion and migration (col. 2, lines 16-20). Hence, the polymer layer mentioned by Otsuka, et al. is not regarded as a rate-controlling membrane (as mentioned by Patnode, et al.). Therefore, as the second/additional adhesive layer disclosed by Patnode, et al. is linked to the presence of a rate-controlling membrane and performs a specific function together with this membrane, and since Otsuka, et al. does not even consider using a rate-controlling membrane, there would have been no motivation for one skilled in the art to have applied any of the teachings of Patnode, et al.

with Otsuka, et al. to arrive at the present invention.

In light of the aforementioned deficiencies of the combination of teachings of Otsuka, et al. and Patnode, et al., the applicant respectfully submits that the combination of references fails to teach every limitation set forth in claims 33-43 and that due to these deficiencies, one skilled in the art would not have been motivated to combine these references to arrive at the present invention. Withdrawal of this rejection is strongly requested.

Turning now to the second rejection under Section 103(a), the applicant respectfully disagrees for at least the numerous aforementioned deficiencies of Otsuka, et al. To reiterate, Otsuka, et al. fails to teach or disclose at least one pressure-sensitive adhesive macromolecular substance layer. Clearly, there would be no motivation to incorporate a “third” macromolecular pressure sensitive drug-containing layer. For the same reason, the applicant respectfully disagrees with the Examiner’s conclusion (referring to Chien, et al.) that “another adhesive layer containing a second drug ... correlates to Otsuka, et al.’s suggested second macromolecular layer.” Regarding Tg values, as discussed above, Otsuka, et al. does not teach or suggest an additional macromolecular layer and if one skilled in the art would have considered the possibility of adding such an additional layer, he or she could not have relied on Otsuka, et al. for selecting a polymer having a suitable Tg value as required by the present invention. Likewise, Chien, et al. does not teach or suggest the Tg values of the polymers present in the adhesive layers. Therefore, applicant respectfully disagrees with the conclusion drawn by the Examiner that “one would have been motivated to utilize another pressure-

sensitive adhesive macromolecular layer, which has a lower glass temperature than the polymer layer” (Office action, page 11, lines 9-11). It is clear that neither Otsuka, et al. or Chien, et al. suggest any teaching relating to the Tg of a putative additional pressure-sensitive adhesive layer.

The Examiner further states that “if a skilled artisan desired to provide a combination therapy wherein one device contained two different drugs, one would have been motivated to use two pressure-sensitive macromolecular layers wherein each respective layer would comprise a different drug” (Office action, page 12, lines 11-13). However, the two-layer composite preparations described by Otsuka, et al. may contain two or more drug substances within one of the layers, as discussed above (col. 2, lines 10-11 “...at least contains therein...;” col. 5, lines 51-52). Therefore, combination therapy could be provided simply by using a combination of active substances within (for instance) the pressure-sensitive macromolecular layer, in accordance with the teaching of Otsuka, et al., and there would be no need for adding a further layer in order to be able to provide a combination therapy.

In light of the deficiencies of the combination of the teachings of Otsuka, et al. and Chien, et al., the applicant respectfully submits that the combination of references fails to teach every limitation set forth in claims 33-43 and that due to these deficiencies, one skilled in the art would not have been motivated to combine these references to arrive at the present invention. It should also be noted that one of the main objectives of the present invention is to reduce cold flow. It is stated in the “Summary of the Invention,” “...it is an object of the invention to provide a process for improving cohesion in order to

achieve a clear reduction of cold flow..." Neither Otsuka, et al., nor Patnode, et al. or Chien, et al. are directed to this object or discuss it in any way. This is yet another reason that these references should not be relied on to support a rejection of the present claims. Withdrawal of this rejection is strongly requested.

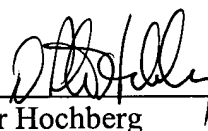
Conclusion

In light of the foregoing claims and arguments, it is believed that the present application is in condition for allowance, and such action is earnestly solicited. The Examiner is invited to call the undersigned if there are any remaining issues to be discussed which could expedite the prosecution of the present application.

Respectfully submitted,

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D. Peter Hochberg Co., L.P.A.
1940 E. 6th St. - 6th Floor
Cleveland, OH 44114
(216) 771-3800
DPH/sm

By: 
D. Peter Hochberg
Reg. No. 24,603